Development of a cell and gene based therapy for hemophilia

Grant Award Details

Development of a cell and gene based therapy for hemophilia

Grant Type: Early Translational IV

Grant Number: TR4-06809

Project Objective: The objective of this DCF ET4 award is to achieve POC that patient-derived, gene-corrected iPSC from hemophilia B patients can be differentiated to hepatocytes, encapsulated in a synthetic matrix, and transplanted ectopically in order to treat Hemophilia B.

Investigator:

Name:	Inder Verma
Institution:	Salk Institute for Biological Studies
Type:	PI

Disease Focus: Blood Disorders, Liver Disease, Pediatrics

Human Stem Cell Use: iPS Cell

Cell Line Generation: iPS Cell

Award Value: $2,298,634

Status: Closed

Progress Reports

Reporting Period: Year 1

View Report

Reporting Period: Year 2

View Report

Reporting Period: Year 3

View Report

Grant Application Details

Application Title: Development of a cell and gene based therapy for hemophilia

Public Abstract: Hemophilia B is a bleeding disorder caused by the lack of FIX in the plasma and affects 1/30,000 males. Patients suffer from recurrent bleeds in soft tissues leading to physical disability in addition to life threatening bleeds. Current treatment (based on FIX infusion) is transient and plagued by increased risk for blood-borne infections (HCV, HIV), high costs and limited availability. This has fueled a search for gene/cell therapy based alternatives. Being the natural site of FIX synthesis, the liver is expected to provide immune-tolerance and easy circulatory access. Liver transplantation is a successful, long-term therapeutic option but is limited by scarcity of donor livers and chronic immunosuppression; making iPSC-based cell therapy an attractive prospect. As part of this project, we plan to generate iPSCs from hemophilic patients that will then be genetically corrected by inserting DNA capable of making FIX. After validation for correction, we will then differentiate these iPSCs into liver cells that can be transplanted into our mouse model of hemophilia that is capable of accepting human hepatocytes and allowing their proliferation. These mice exhibit disease symptoms similar to human patients and we propose that by injecting our corrected liver cells they will exhibit normal clotting as measured by various biochemical and physiological assays. If successful, this will provide a long-term cure for hemophilia and other liver diseases.

Statement of Benefit to California: Generation of iPSCs from adult cells unlocked the potential of tissue engineering, replacement and cell transplant therapies to cure a host of debilitating diseases without the ethical concerns of working with embryos or the practical problems of immune-rejection. We aim to develop a POC for a novel cell- and gene-therapy based approach towards the treatment of hemophilia B. In addition to the obvious and direct benefit to the affected patients and families by providing a potential long-term cure; the successful development of our proposal will serve as a POC for moving other iPSC-based therapies to the clinic. Our proposal also has the potential to treat a host of other hepatic diseases like alpha-1-antitrypsin deficiency, Wilson's disease, hereditary hypercholesterolemia, etc. These diseases have devastating effects on the patients in addition to the huge financial drain on the State in terms of the healthcare costs. There is a pressing need to find effective solutions to such chronic health problems in the current socio-economic climate. The work proposed here seeks to redress this by developing cures for diseases that, if left untreated, require substantial, prolonged medical expenditures and cause increased suffering to patients. Being global leaders in these technologies, we are ideally suited to this task, which will establish the state of California at the forefront of medical breakthroughs and strengthen its biomedical/biotechnology industries.